EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY (ESWL) FOR UPPER URINARY STONES IN ADULTS AND IN CHILDREN

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1. INTRODUCTION

Extracorporeal generated shock waves have been introduced for medical therapy approximately 20 years ago to disintegrate kidney stones. This was a landmark in the history of urinary tract stone therapy.

During the Second World War it was observed that the lung of castaways was cracked because of the explosion of waterbombs, although no outer symptoms of violence existed. This was the first time that the influence of shock waves on tissue was observed.
In 1966 during experiments with high velocity projectiles performed by Dornier Company, an employee touched the plate at the very moment where the projectile hit the plate. He felt something in his body like an electrical shock. Measurements show that no electricity was present. The generated shock wave travelled from the plate, over the hand into the body. From 1968 the shock wave effect on biological tissue in animals was investigated in Germany, financed by the Department of Defence. These investigations lead to the idea to disintegrate kidney stones with extracorporeal generated shock waves. In 1971 Haeusler and Kiefer reported about the first in-vitro disintegration of a kidney stone with shock waves without direct contact to the stone. In 1974 the Department of Research and Science of Germany financed the research program "Application of the ESWL" with participants Eisenberger, Chaussy, Brendel, Forßmann and Hepp. In February 1980 the first patient with a kidney stone was treated in Munich with a prototype machine called Dornier Lithotripter HM1 (Human Model 1).
In 1983 the first commercial lithotripter (Dornier HM3) was installed in Stuttgart, Germany. Today the treatment of kidney and ureteric stones with extracorporeal shock waves is the first treatment of choice. More than 10 Million patients have been treated since that.

The basic mechanism of SWL is that extracorporally generated, focused shock wave can fragment urinary calculi into small pieces. The pieces pass along the ureter and voided in the urine via the urethra. Shock waves are transported into the body by water. Modern lithotripters work without a bathtub and without anaesthesia. For localization of stones, lithotripters are equipped with x-ray and/or ultrasound localization systems.

Shock waves are acoustic waves, characterized by a single high positive pressure front and a negative tensile wave afterward. The positive pressure is responsible for the direct shock wave effect and the tensile wave for the cavitation, which is called the indirect shock wave effect. The very fast pressure transition of shock waves causes very high tension at the interfaces (i.e. water – stone) so that the structure of the material cracks.

The tensile part of a shock wave corresponds to a local lowering of the pressure so that cavitation bubbles will be created; these bubbles are growing under the influence of the tensile wave. After a certain time the bubbles collapse uncontrolled. The interaction between shock waves and gas bubbles attached to a surface generates water jets and a hole will be created on the surface of the stone. The disintegration of a kidney stone is a combination between direct and indirect shock wave effect.

Histological studies in experimental animals and clinical experiences showed that ESWL could damage renal tissues and, at least acutely impair renal function. Depending on the energy density, first venules are damaged in the medulla, followed by rupture of arterioles in the renal cortex. CT and MRI have demonstrated intrarenal and perirenal haemorrhage in humans. Determination of urinary enzymes as non-invasive tests of renal functional integrity provides a very sensitive indicator of renal damage. The transient significant increase in excretion of several urinary enzymes (ASAT, ALAT, NAG, ALP and LDH) and low molecular weight proteins such as albumin and β-2 microglobulin following ESWL have been well demonstrated in adults, but there are very few clinical data about the bioeffect of ESWL in children. Renal impairment after ESWL may be greater in pediatric patients than in mature patients determined by anatomical and physiological characteristics of immature tissues.

2. AIM

1. SWL is the first treatment of choice for most urinary calculi in adults. Our aim was to review the outcomes of SWL in cases of kidney stones in adult population. We clarified the correlations between the stone size and the stone free rate, effectivity and complication rate to help on more precise selection of the patient for the treatment. .

2. In children the SWL technique has now been in limited use for more than 10 years. Our goal was to prove the clinical safety and efficacy of extracorporeal shock wave lithotripsy in pediatric population. Based on our results we determined the optimal treatment settings, technical parameters and strategy in childhood.

3. In spite of numerous studies, the biologic effect of ESWL on the immature kidney has not yet been evaluated. No data was found in the literature discussing the functional disorders in children following SWL. Our goal was to detect the short-term effect of ESWL on renal function in children measured by biochemical parameters. The degree and he duration of the disorder was discussed.

3. EFFICACY OF ESWL TREATMENT FOR UPPER URINARY TRACT STONES IN ADULT

3.1. Patients and method

Data of 1070 adult patients treated by ESWL for solitary kidney stone between 1 February 1993 and 31 December 2000 were analyzed retrospectively. We analyzed the data of those patients whose clinical and radiological documentation were available including stone analysis and follow-up for at least one year. 1328 treatments were performed for 1070 stones by Dornier Compact device under ultrasound guidance. After ESWL all patients were evaluated at regular intervals (2 week, 1 month, 3 months after treatment and at 6-month intervals).

Patients were divided into two groups based on the stone composition requiring different treatment strategies: Group I with Ca containing stones and group II with uric acid (UA) containing stones.

In Group I 1146 ESWL treatments were performed for 926 solitary Ca containing kidney stones in three subgroups according to the stone size: smaller than 10 mm, between 10-20 mm and larger than 10 mm.

In Group II 199 ESWL treatments were performed for 144 UA containing kidney stone patients. The chemical composition was pure (100%) UA in 87 cases and mixed (containing at least 60% UA) in 57 cases. After ESWL and between the repeated treatments the conventional medication was applied: alkalization of the urine by oral citrate application (to pH 6.5-7) and reduction of UA excretion by giving allopurinol (1-3 x 100 mg /day). Stones were divided into two subgroups according to the stone size: between 10-20 mm and larger than 20 mm.

Treatments were considered successful, when stones were fragmented and cleared, rendering the patient stone-free or with insignificant residual fragments <4 mm.

We stratified our results according to the stone composition and size. The stone free rates, the effectivity quotient (EQ), the retreatment rate, and the auxiliary procedures necessitated by complications were analyzed and compared in each groups and subgroups.

3.2. Results

69% of patients with Ca containing stones smaller then 10 mm became stone free within 1 month, the ratio increased to 95% after 6 month. In cases of stone size between 10-20 mm, the stone free rate was less favourable. Patients with stone larger than 20 mm became stone free to six month, but only in 52 %. The ratio of the auxiliary procedures was only 2% in subgroup 1, in contradiction to 26% in subgroup 3. Details are shown in the Table.

Stone size	**Stone free**		**Re ESWL (%)**	**Resid. fragm. (%)**	**Auxiliary procedures (%)**	**EQ (%)**
	No	**%**				
<10 mm	613	95	14	3	2	82
10-20 mm	206	86.6	33	7	7	62
>20 mm	22	52	116	22	26	23
Total	**841**	**91**	**23**	**5**	**4**	**71**

Similar relations were observed in Group II. The session number and dissolving time correlated with the size of the stone, but even larger pure uric acid stones were dissolved successfully using the combined strategy. Mixed stones were partly resistant to combined therapy. Direct correlation was detected between treatment failure and the amount of non-UA stone components. Details are shown in the Table.

Stone type and size	**Stone free**		**Re ESWL (%)**	**Resid. fragm. (%)**	**Auxiliary procedures (%)**	**EQ (%)**
	No	**%**				
Pure UA	82	94	29	1	5	70
10-20 mm	57	98.3	20	0	1,7	81
>20 mm	25	86	45	3	10,3	54.3
Mixed UA	47	82	52	7	10,5	48.4
10-20 m	32	86	43	5	8,1	55
>20 mm	15	75	70	10	15	38.5
Total	**129**	**89.6**	**38**	**3,5**	**7**	**60.3**

3.3. Conclusions

Based on our data, the ESWL treatment seems to be safe, effective and minimally invasive in adult patients. Analyzing the treatment results of 1070 solitary kidney stones, the total stone free rate was 90.6% and the effectivity quotient was 69.6%. The auxiliary procedures rate was favourable - 5%. In patients with Ca containing stone the treatment results correlate with the stone size. The stone free rate and the effectivity quotient correlated in inverse ratio to stone size. The retreatment rate and number of auxiliary procedures increased in direct ratio to the stone size, with a maximum in subgroup of stones larger than 20 mm. In the latter case the primary ESWL treatment is not recommended because of the low success rate (SF: 57%, EQ: 24%), and the relatively higher complication rate (auxiliary procedures rate: 33%).

Making comparison between the results of the two groups a better outcome (higher stone free rate, lower retreatment and complication rate) was observed in Group II especially in cases of larger stones. ESWL increases the effectivity of medical therapy, because increased surface area of the disintegrated stone comes in touch with alkalinized urine. On the other hand, by disintegration of stone, inside UA layers became accessible for dissolving agents, resulting in better dissolving effect, shorter dissolving time and low complication rate.

4. APPLICATION OF SHOCK WAVE LITHOTRIPSY IN PEDIATRIC POPULATION

4.1. Patients and method

Between February 1993 and December 2005, 104 children with 129 urinary stones (95 renal, 34 ureteric stone) were treated with the second generation Dornier Compact lithotripter. There were 55 boys 49 girls with a mean age of 10.3 (4–l6) years.

Treatments were given under ultrasound guidance in 139 SWL sessions for 95 renal, 8 upper ureteric, 3 middle ureteric and 23 lower ureteric stones.

The mean stone size was 11.4 mm (4.8–22.5 mm). The number of shock waves per stone averaged 2510 (1489-3200). The mean size of ureteric stones was 12.1 mm, the

average shock wave number was 2830 (2500–3500). Shock wave energy settings ranged from 11 to 13 kV. Treatments were considered successful, when stones were fragmented and cleared, rendering the patient stone-free or with insignificant residual fragments < 3 mm.

The stone free rate, the efficacy quotient and the complication rate was calculated. The history of the patients, the stone composition and the stone recurrence was analyzed with a median 6.64 years follow-up.

4.2. Results

The overall stone-free rate was (91.5 %) and the efficiency quotient (EQ) was 82.5 % at 3 months after SWL. The complication rate was favourable - 3.1 %. Results are summarized in Table.

	Kidney	**Ureter**	**Total**
N^{o} stones	95	34	**129**
N^{o} stone free	86	32	**118**
N^{o} retreatment	7	3	**10**
Residual fragment >3 mm	7	0	**7**
Auxiliary procedures	0	0	**0**
Secondary operation	2 PCNL	2 URS	**4**
EQ (%)	**82.6**	**82**	**82.5**

Documented stone forming risk factor was fond in 44 patients (42.3%): metabolic disorder was found in 30 patients (hypercalciuria, hypomagnesiuria, cystinuria), anatomic alteration in 13 patients, infect origin in 6 cases, familiar in 5 cases.

Stone analysis was performed in 80 patients. The result was: Ca oxalate dihydrate alone in 59% and Ca oxalate dihydrate in combination with monohydrate in 19%, struvit in 5 % and cystine in 4 % of the cases. The stone recurrence rate was 14 %.

4.3. Conclusions

ESWL in children requires special technical adaptation and modifications of treatment. The treatment should be effective but protective. The technical parameters of each ESWL machines are very different, but second or third generation, ultrasound guided

machines with small focal zone are recommended for the treatment.

Technically, the flat table of the device permitted easier positioning. The small focal zone is optimal to minimize the injuries of surrounding organs. In our practice there was no need for lung shielding.

According to our experience, the real-time monitoring via ultrasound during the treatment enabled prompt correction of positioning and resulted in a decrease in retreatment rate and in shock numbers. On the other hand, by using ultrasound guidance, the radiation exposure could be removed. More precise focusing results in less parenchyma injury.

Experienced urologist must perform the treatment. The power setting and shock wave number should be kept to as low as possible but high enough to reach optimal disintegration. In childhood the calcium oxalate dihydrate stones are the most common, which disintegrate at lower energy.

Stone fragments passed faster and with fewer complications in children than in adults. On the other hand, children had a better stone clearance rate than adults at the same interval due to shorter stone lodge, more rapid and better mobilization after treatment.

In our series the overall success rate was favourable. The retreatment rate is lower than those reported in other paediatrics series. The complication rate and secondary operation number was low, but endoscopic background and experiences operator was mandatory. In conclusion, SWL using ultrasound guided Dornier Compact lithotripter is an effective treatment of most urinary stones in children. Because of the high success rate and the low risk of complications, lithotripsy can be applied as an outpatient treatment modality in children over 4 years of age. In nearly half of the cases a predisposing factor for stone formation can be found in children, and the stone recurrence rate is higher than in adult population. Detailed physical and laboratory examinations, analysis of the calculus can help to evaluate the causes. Regular follow-up and preventive medical therapy is required.

5. SHORT –TERM CHANGES IN RENAL FUNCTION FOLLOWING ESWL IN CHILDREN

5.1. Patients and method

In 16 children (8 boys, 8 girls) aged 6-12 (mean 9.6 years) treated at our department,

the short-term effect of ESWL was studied measuring changes of biochemical markers in a 12-month period. The children were treated for single kidney stones in the first session under general anaesthesia. The mean stone size was 8.2 mm (range 6 –12), 9 stones were on the left side, 7 on the right side. Treatments were done under continuous real-time US monitoring controlled by the same urologist. The number of shock waves per stone averaged 2360 (1420–2700). Shock wave energy settings ranged from 11 kV to 13 kV. Children with concomitant diseases, urogenital tract abnormalities and previous operation on the urogenital tract or uroinfection were excluded from the study.

Over the routine follow-up procedures excretion of electrolytes (Na, K, urea, creatinine), β-2 microglobulin and urinary activities of ASAT, ALAT, ALP, LDH were checked as well as different serum parameters (Na, K, urea, creatinine levels). Serum C-reactive protein (CRP) was determined to detect acute infection.

Samples were collected immediately before and 2 hours after ESWL, and on days 1, 2, 8, 15, 30 and 90 following the treatment.

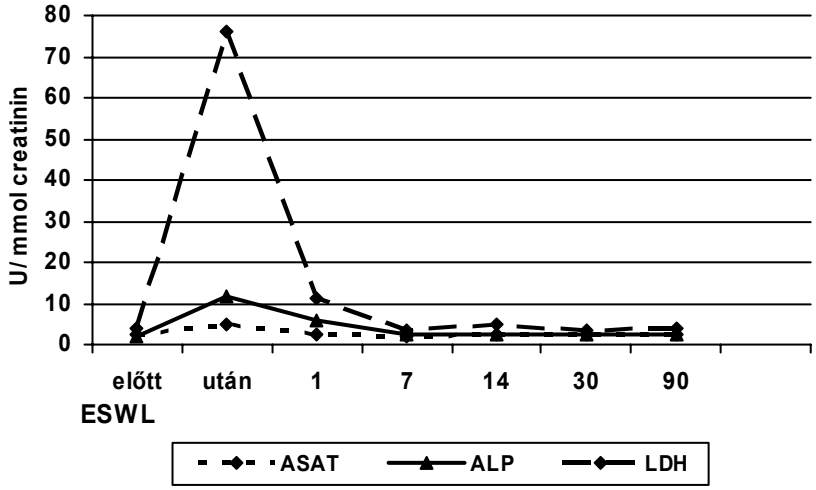
Urinary enzyme levels were reported in relation to urinary creatinine concentration. The results were expressed as mean +/- standard error of mean. Pre-treatment levels were considered as a baseline. Statistical analysis of data was made by paired t-test. P values less than 0.05 were considered significant.

5.2. Results

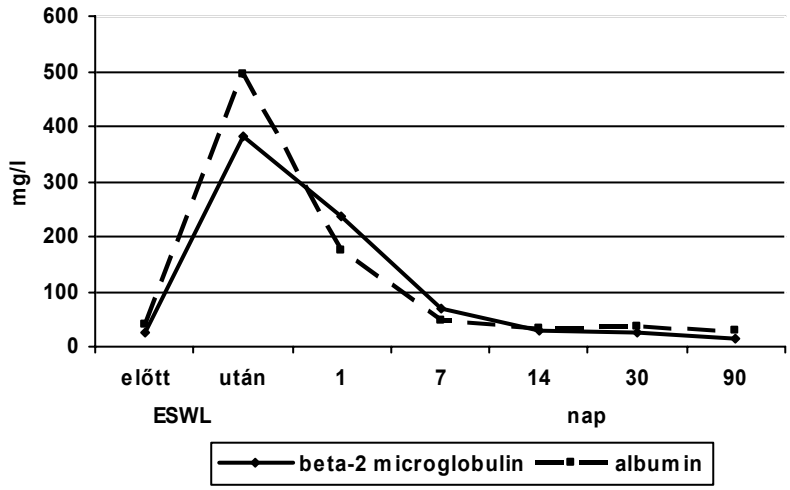
The overall renal function (serum Na, K, urea, creatinine levels) and urinary excretion of electrolytes remained stable. CRP remained within the normal range excluding urinary and non-urinary infections.

The excretion of ALAT remained unaltered. A mild elevation of ASAT ($p < 0.01$) excretion was detected after the ESWL, returning to the baseline level to the 7th day.

ALP was increased at a five-fold level relative to baseline immediately after the treatment ($p<0.01$), and stayed elevated until the 7th day. The LDH excretion increased extremely, more than twenty-fold ($p <0.001$) relative to pre-treatment value 2 hours after the ESWL, it remained high on first day, then showed a rapid decrease to 7th day. Pre-treatment value was reached at the 14th day. Details are shown on picture.



A marked increase of albumin and β-2 microglobulin level occurred 2 hours after the treatment ($p < 0.001$) and on first day ($p < 0.01$). On the seventh day, only a mild but significant elevation was found ($p < 0.02$), and the excretion decreased to the baseline level on the 14th day. Details are shown on picture.



5.3. Conclusions

Theoretically the higher water content of immature tissues can result in increased possibility of cavitation and jet effect and better shock wave extension into soft tissues. The smaller size of organs can result in wider propagation of shock wave energy existing as a possible risk factor of trauma of the neighbouring organs. Owing to these facts, children can

be more susceptible for SW hazard.

Macroscopic alterations of the treated region (haematoma of the kidney or neighbouring organs) were not observed at our series, and the overall renal function remained stable.

Urinary loss of different enzymes and proteins was detected following ESWL, originated from transient disorder of the kidney. No previous data have been found in the literature studying functional changes of renal function in children. Our study documents a transient renal proximal tubular dysfunction in children.

A mild and short-duration elevation of the cytoplasmic enzyme ASAT was found. No difference was detected according to the sex and side. No change was observed in urinary levels of ALAT of mitochondrial origin. These data correlate with ultrastructural findings showing vacuolization of cytoplasm and disruption of cell membranes. Mitochondria seem to be more resistant to SW energy.

The dramatically elevated LDH level in urine denotes cellular damage of the kidney and surrounding muscles as well. In comparison with girls, a more prominent elevation of LDH was detected in boys whose musculature is generally stronger. It is known that 10-20 % of SW energy is lost through the skeletal muscles.

The increase of the brush border enzyme ALP is an indicator of proximal tubular dysfunction. The elevation of it was detectable at least two weeks after treatment as well as β-2 microglobulin.

Post-treatment elevation of albumin and β-2 microglobulin was described in several studies, but enhancement of albumin excretion is partially due to haematuria after the treatment. The β-2 microglobulin normally freely filtered glomerularly and almost completely reabsorbed in the proximal tubule. The elevated β-2 microglobulin levels in urine samples after ESWL indicate incomplete reabsorption which can result from either a functional alteration of proximal tubular permeability or more likely a direct mechanical effects, namely membrane rupture which regenerates within two weeks.

The longer regeneration time of tubular function in children in comparison to adults (14 days versus 7 days) shows that ESWL can be more detrimental on growing organs. To reduce the possibility of more serious or prolonged functional disorders, we suggest waiting minimally 2 weeks until renal function normalize before repeated ESWL or other operation.

6. THESIS

1. ESWL is the primary treatment option for most urinary stones. Analyzing the treatment results of 1070 solitary kidney stones, the total stone free rate was 90.6% and the effectivity quotient was 69.6%. The auxiliary procedures rate was favourable - 5 %.

2. The stone free rate and the effectivity quotient correlated in inverse ratio to stone size. The retreatment rate and number of auxiliary procedure increased in direct ratio to the stone size, with a maximum in subgroup of stones larger than 20 mm.

3. In this cases of stones larger than 20 mm the primary ESWL treatment is not recommended because of the low success rate (SF: 57 %, EQ: 24%), and the relatively higher complication rate (auxiliary procedures rate: 33%).

4. Even larger pure uric acid stones were dissolved using combined (ESWL + dissolving therapy) treatment. The session number and the dissolving time correlated with the size of the stone. ESWL improved the effectivity of medical therapy, because increased surface area of the disintegrated stone comes in touch with alkalinized urine.

5. SWL using ultrasound guided Dornier Compact lithotripter is an effective treatment for most urinary tract stones in children. Based on the treatment result of 104 children (4-16 age), the overall stone-free rate was (91.5 %) and the efficiency quotient (EQ) was 82.5 % The complication rate was favourable - 3.1 %.

6. The special technical adaptation and modifications required for effective but protective SWL treatment of children are discussed. The conditions of optimal treatment are: :
   - machine related (small focal zone, US imaging)
   - patient related (age, stone size, position and composition)
   - operator related (adequate treatment strategy including limitation of power setting and shock wave number, experience, endoscopic background, follow-up).

7. Documented stone forming risk factors were fond in 44 patients (42.3%): metabolic disorder was found in one third of the patients, anatomic alteration in one quarter of

patients, infect origin and familiar causes in 10%. Stone analysis was performed in 80 patients. The stone recurrence rate was 14 % despite of adequate prophylactic treatment.

8. No data was found in the literature discussing the functional disorders in children following SWL. Analyzing different urinary enzyme leakage and albumin and β-2 microglobulin levels in the urine I documented a transient renal proximal tubular dysfunction in children following SWL. The data indicates either a functional alteration of proximal tubular permeability or more likely direct mechanical effects, namely membrane rupture which regenerates within two weeks.

9. The longer regeneration time of tubular function in children in comparison to adults (14 days versus 7 days) shows that ESWL can be more detrimental on growing organs. Considering the functional regeneration time, we suggest to wait minimally 14 days before repeated ESWL or other operation

A TÉMÁBAN MEGJELENT KÖZLEMÉNYEK ÉS ELŐADÁSOK

KÖZLEMÉNYEK

1. **Villányi K. K.,** Székely J. G., Götz F., Jávor E.: ESWL treatment and it's short-term effect on renal function in children. J. Endourol. Suppl. **9:** 104, 1995. **IF: 0,994**

2. **Villányi K.,** Pusztai Cs., Székely J., Götz F.: Húgyúti kövek ESWL kezelése gyermekkorban. Orv. Hetil. **137**: 1029-1031, 1996.

3. **Villányi K. K**., Székely J. G., Buzogány I., Götz F.: Experiences with the management of pediatric urolithiasis during a 5-year period. J. Endourol. Suppl. **12:** 119, 1998. **IF: 0,998**

4. Pusztai Cs,, **Villányi K. K.,** Farkas L., Buzogány I.: In situ ultrasound guided SWL of ureteral stones: impact of stone position on the efficacy. J. Endourol. Suppl. 13: 51, 1999. **IF: 1,02**

5. Pusztai Cs., **Villányi K. K.,** Farkas L., Buzogány I.: In situ ultrasound guided SWL of ureteral stones: impact of stone size on the efficacy. J. Endourol. Suppl. 13: 52, 1999. **IF:1,02**

6. Székely J. G., Farkas L.M., **Villányi K. K.,** Somogyi L., Beöthe T. Z.: Endopyelotomy for horseshoe and ectopic kidneys. J. Urol. **161:** 1914-1915, 1999. **IF: 2,486**

7. **Villányi K. K.,** Pusztai Cs., Székely J.G., Farkas L.: Combined treatment of uric acid containing upper tract urinary stones. J. Endourol. Suppl. 14: 82, 2000. **IF: 1,112**

8. **Villányi K. K.**, Székely J.G., Farkas L. M., Jávor E., Pusztai Cs.: Short-term changes in renal function following extracorporeal shoch wave lithotripsy in children. J. Urol. **166**: 222-224, 2001. **IF: 3,19; Citáció: 6**

9. **Villányi K.,** Székely J., Farkas L., Tornai Z.: A gyermekkorban végzett ESWL kezelés stratégiájáról. Magy. Urol. **13**: 129-133, 2001.

10. **Villányi K. K.**, Pusztai Cs., Székely J.G., Farkas L.: SWL in children: efficacy and long-term follow-up. J. Endourol. Suppl. **19:** 105, 2005.**IF: 1,552**

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ELŐDÁSOK

1. **Villányi K.,** Pusztai Cs., Götz F.: ESWL kezelés gyermekkorban. Magyar Urológus Társaság 9. Kongresszusa, Budapest 1994. okt. 13 – 15.

2. **Villányi K.:** Az első 1000 ESWL kezeléssel szerzett tapasztalataink. POTE Urol. Klin. Jubileumi Tudományos Ülése Pécs, 1995.

3. **Villányi K.,** Székely J., Jávor A.-né: ESWL kezelés hatása a veseműködésre gyermekkorban. Magyar Urológus Társaság 10. Kongresszusa, Debrecen 1997. okt. 16–18.

4. **Villányi K.**: Műtéti beavatkozások és kőrecidiva összefüggése. Huth Tivadar Urológus Napok, Pécs, 1998. szept. 17–18.

5. **Villányi K.:** ESWL kezelés gyermekkorban. Felkért előadás, Szakorvosi Továbbképzés HIETE Budapest 1998 nov.17.

6. **Villányi K**.: ESWL – technikai háttér, kezelési mód, eredmények. Felkért előadás, Szakorvosi Továbbképzés Semmelweis Egyetem Budapest 2000. dec. 05.

7. **Villányi K**.: Kőbetegség gyermekkorban. Felkért előadás, Gyermeksebészeti Továbbképző Tanfolyam, Pécs, 2005. Szeptember 19-20.

8. **Villányi K.:** Vesekövesség gyermekkorban. Felkért előadás. FUN, Semmelweis Egyetem 2005.

9. **Villányi K.:** Vesekövesség gyermekkorban. Felkért előadás. Távoktatási program, 2006.

EGYÉB KÖZLEMÉNYEK ÉS ELŐADÁSOK

KÖZLEMÉNYEK

1. Pintér J., Szokoly V., **Villányi K.,** Böszörményi-Nagy G.: Vesedaganat eltávolítása extrapleurális thoracoabdominális feltárásból. Urol. Nephrol. Szle. **14/2**: 77-83, 1987.

2. Pintér J., Szokoly V., **Villányi K.,** Böszörményi-Nagy G.: Removal of renal tumours from thoracoabdominal incision. Acta Chirurg. Hung. **28:** 209-215, 1987.

3. Böszörményi-Nagy G., **Villányi K.**: Epidurális anesztéziában végzett Zeiss hurkos kőextrakciók. Urol. Nephrol. Szle. **15/3:** 133-138, 1988.

4. Fehér M., Bedri I., Böszörményi-Nagy G., **Villányi K.**: Vascular anomalies and retroperitoneal lymphadenectomy (RLA). Acta Chirurg. Hung. **29:** 269-272, 1988.

5. Varga A., **Villányi K.**, Erdei K., Böszörményi-Nagy G.: A hólyagdaganatok kezelésének szempontjai Klinikánkon. Magy. Urol. **1:** 23-29, 1989.

6. Szokoly V., Pintér J., **Villányi K.**: A világossejtes veserák diagnosztikájának és terápiájának néhány kérdése. Magyar Radiológia **63**: 283-287, 1989.

7. **Villányi K.**, Soltész I., Szokoly V., Varga A.: A hypospadiasis korrekciós műtéteiről. Magy. Urol. **1:** 39-47, 1989.

8. **Villányi K.**, Szokoly V., Flaskó T.: A vesedaganatos betegek túlélése a v. cavában lévő tumor-thrombus esetén. Magy. Urol. **2**: 275-283, 1990.

9. Böszörményi-Nagy G., **Villányi K**.: Akut veseelváltozások ultrahang-diagnosztikája. Magy. Urol. **3:** 35-47, 1991.

10. **Villányi K.,** Böszörményi-Nagy G. : Vese-cystapunkciók. Magy. Urol. **3:** 59-65, 1991.

11. **Villányi K**., Böszörményi-Nagy G,. Berényi P.: A retroperitoneum ultrahangvizsgálata. Magy. Urol. Suppl. 3: 1-9 1991.

12. Varga A., Szokoly V., **Villányi K.,** Böszörményi-Nagy G.: Vizeletdeviációs módszerek és indikációjuk. Magy. Urol. **3:** 133-139, 1991.

13. Böszörményi-Nagy G., **Villányi K.,** Berényi P.: A longitudinális rectalis és vaginális UH-vizsgálatok értéke az urológiai diagnosztikában. Magy. Urol. Suppl. **3:** 45-53, 1991.

14. Pintér J., **Villányi K.,** Szokoly V.: Szervmegtartó műtétek a rosszindulatú vesedaganatok gyógykezelésében. Magy. Urol. **4**: 17-33, 1992.

15. Szokoly V., Böszörményi -Nagy G., **Villányi K.:** A pyelo-ureteralis szűkületek klinikuma és terápiája Magy. Urol. **4:** 131-141, 1992.

16. J.G. Székely, **K. K**. **Villányi,** L. Farkas: Percutaneous nephropexy, a new endoscopic procedure for the treatment of renal ptosis. J. Endourol. Suppl. **9:** 107, 1995**.**
IF: 0,994

17. L. Farkas, J.G. Székely, **K. K. Villányi**: Experiences in endoscopic treatment of upper urinary tract uroepithelial tumors. J. Endourol. Suppl. **9**: 117, 1995.
IF: 0,994

18. Jilling Á., **Villányi K.,** Farkas J.: A férfi vizelet inkontinentia műtéti megoldása. Magy Urol. **4:** 339-403, 1996.

19. Székely J., Somogyi L., **Villányi K.:** Kezdeti tapasztalataink urothelialis neoplasticus folyamatok kimutatásával 5-amino-levulinsav intravesicalis instillatióját követően. LAM **8(4):** 276-279, 1998.

20. Székely J.G., **Villányi K.,** Battyány I.: Technical aspects of percutaneous renal biopsy now (letter). Nephron, **79:** 106, 1998. **IF: 1,696** **Citáció: 1**

21. Székely J.G., Farkas L., **Villányi K.**: Possibilities to improve the effectivity of endopyelotomy. J. Endourol. Suppl. **12**: 132, 1998. **IF: 0,998**

22. Szekely JG, Farkas LM, **Villanyi KK**, et al.: Endopyelotomy for horseshoe and ectopic kidneys. J.Urol. **161:**1914, 1999. IF:

23. **Villányi K.:** A vesedaganatok kezelése. Orv. Hetil. **146/8**: 377-379, 2005.

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Összesített publikációs index: 7,69

ELÔADÁSOK

1. Szokoly V., Böszöményi-Nagy G., **Villányi K.,** Pintér J.: Extrapleurális thoracoabdominális feltárás vesetumor eltávolítására (poszter). Magy. Onkol. Társ. XVII. Kongr. Budapest 1987. nov. 12-14.

2. Böszörményi-Nagy G., **Villányi K.,** Korányi L.: Regionális anesztézia alkalmazása az urológiai sebészetben. DOTE Urol. Kl. Tudományos Ülése Debrecen, l988. márc. 28.

3. **Villányi K.**, Szokoly V., Pintér J.: Előrehaladott vesedaganatok műtéti kezelése. DOTE Urol. Kl. Tudományos Ülése Debrecen, l988. márc. 28.

4. Böszörményi-Nagy G., Berényi P., **Villányi K.,** Szokoly V.: Az ultrahang szerepe a vese daganatos megbetegedéseinek diagnosztikájában és terápiájában. Tudományos Ülés, Szeged 1989. nov. 3.

5. **Villányi K.,** Böszörményi-Nagy G.: A retroperitoneum ulrahangvizsgálata. Magyar Radiol. Társ. Kongresszusa, Debrecen 1992. máj. 25-27.

6. Böszörményi-Nagy G., **Villányi K.:** Acut veseelváltozások ultrahang diagnosztikájának egyes kérdései. Magyar Radiol. Társ. Kongresszusa, Debrecen 1992. máj. 25-27.

7. **Villányi K.,** Böszörményi–Nagy G., Berényi P.: A modern képalkotó eljárások szerepe a vesedaganatok műtéteinek tervezésében. Felkért előadás, SOTE Szakorvos Továbbképés, Budapest, 1993. szept. 20.

8. **Villányi K. K.**, Székely J. G., Farkas L.: Endocalycotomy. Videofilm, Congress of Video-Urology, Athens, Greece 1994. –**3. díjat nyert.**

9. Székely J.G., **Villányi K. K.**, Farkas L.: Percutaneous nephropexy. Videofilm, Congress of Video-urology, Athens, Greece 1994.

10. **Villányi K.** , Székely J., Farkas L.: Endocalycotomia. Videofolm, Magyar Urológus Társaság 9. Kongresszusa, Budapest 1994. okt. 13-15.

11. Buzogány I., **Villányi K.,** Magyarlaki T., Schuth J.: Ambulanter Interferon alfa Therapie bei metastasierem Nierenzellkarzinom. Phase II Studie. III. Wissentschaftliche Tagung der Südostdeutschen Gesellschaft für Urologie München, 1995 jún. 15 –17.

12. Buzogány I., Magyarlaki T., **Villányi K.,** Polyák L., Mosonits Sz.: Prognosztikus immunhisztikémiai markerek vizsgálata immunkezelt vesedaganatban.Magyar Onkológusok Társasága XXI. Kongr. Pécs, 1995. nov. 9-11.

13. Buzogány I., **Villányi K.,** Polyák L., Götz F.: Az előrehaladott vesecarcinoma kezelésének elve és gyakorlata. Magyar Onkológuso Társasága XXI. Kongr. Pécs, 1995. nov. 9-11.

14. **Villányi K.,** Buzogány I., Polyák L., Götz F.: Vesedaganat miatt végzett biokemotherápia. Magyar Onkológusok Társasága XXI. Kongr. Pécs, 1995. nov. 9-11.

15. **Villányi K.:** A vesevezeték műtéteiről. Továbbképző előadás. Bajai Urológus napok, Baja 1996.

16. Buzogány I., Magyarlaki T., **Villányi K.,** Csanaky Gy., Szereday Z.: Angiomyolipoma és vesesejtes rák együttes előfordulása (poszter). Magyar Urológus Társaság 10. Kongresszusa, Debrecen 1997. okt. 16–18.

17. **Villányi K.:** A kismedence szervei: ureter, húgyhólyag, prostata, rectum. Szakorvosi Felkészítő és Továbbképző program 2002. jan. 23-25. Pécs

18. **Villányi K.:** Az előadás, poszterkészítés irányelvei. Szakorvosi Felkészítő és Továbbképző program 2002. jan. 23-25. Pécs

19. **Villányi K**.: Endocalycotomia, infundibulotomia. Szakorvosi Felkészítő és Továbbképző program 2002. nov. 20-23. Pécs

20. **Villányi K.:** Az előrehaladott stádiumú PC hormonkezelésének elve és gyakorlata. Szakorvosi Felkészítő és Továbbképző program 2003. máj. 28-30. Pécs

21. **Villányi K.:**ESWL kezelés felnőtt és gyermek korban. IV. Huth Tivadar Urológus Napok 2002. jun. 26-27. Pécs

22. Székely J., **Villányi K.,** F. Bagheri: Cirkuláris drénnel végzett percutan nephropexia hosszú távú eredményei. MUT XII. Kongresszusa 2003 szept. 11-12. Szeged

KÖSZÖNETNYILVÁNÍTÁS

Bellyei Árpád professzor úrnak köszönöm, hogy PhD programjába kerülésemmel megteremtődtek értekezésem megírásához szükséges feltételek.

Farkas László egyetemi tanárnak, intézetvezetőmnek köszönöm, hogy a szoros rutin klinikai tevékenység és oktatási terhek mellett lehetőségem nyílt a beteganyag tudományos feldolgozására.

Götz Frigyes emeritus professzornak, témavezetőmnek, hálás vagyok útmutató bölcs tanácsaiért.

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